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mannosylated adj poly adj L adj lysine	6

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USPT	mannosylated adj poly adj L adj lysine	6	<u>L8</u>
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USPT	interleukin adj 2 same hypoxia	1	<u>L1</u>

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L1: Entry 1 of 1

File: USPT

Aug 24, 1999

DOCUMENT-IDENTIFIER: US 5942434 A  
TITLE: Nucleic acid constructs comprising hypoxia response elements

BSPR:

A second example of a hypoxia-associated regulator is a regulator which lies 5' to the mouse phosphoglycerate kinase gene promoter. The sequence of the regulator has been published (McBurney et al, 1991) but its hypoxia inducible properties have not previously been considered or defined in the literature. It has now been recognised by the inventors that the native sequence of the regulator has hypoxically-inducible features. The nucleotides responsible have been defined and the inventors have shown that repeating the sequence leads to increased induction of the gene whose expression is controlled. Further, the inventors have shown that using the interleukin-2 gene under tissue-specific promoters is an effective strategy for specific targeting of tumours.

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L8: Entry 3 of 6

File: USPT

Oct 26, 1999

DOCUMENT-IDENTIFIER: US 5972900 A  
TITLE: Delivery of nucleic acid to cells

DRPR:

FIG. 3--Tissue specificity of mannosylated DNA complex in targeting DNA to the macrophages in vivo. Mannosylated poly-L-lysine was conjugated to SV40/luciferase DNA. 300 .mu.g of the DNA complex were introduced into the caudal vena cava of rats. Four days after injection tissue extracts were made and assayed for luciferase activity. The luciferase activity is plotted as Integrated Light Units per milligram of protein extract from spleen, liver and lung. In other tissues no activity was found. Data are expressed as means. $\pm$  standard error of the mean (SEM). The light bars are the non-transfected controls (n=4), and the dark bars, animals transfected with mannosylated poly-L-lysine/DNA complexes (n=5).

DRPR:

FIG. 4--Specificity of mannosylated DNA complex in targeting DNA to primary culture of macrophages in vitro. Primary cultures of peritoneal macrophages were transfected with either galactosylated poly-L-lysine (light bars) or mannosylated poly-L-lysine (dark bars) conjugated to a SV40/luciferase DNA. At the indicated times (2, 4, 8, and 24 hours) cells were washed. Twenty-four hours after transfection, cells were harvested and assayed for luciferase activity. The luciferase activity is plotted as Relative Luciferase Activity after being standardized by the activity found in untransfected controls. Data are expressed as means. $\pm$  standard error of the mean (SEM).

DRPR:

FIG. 5--Competition between the mannosylated DNA complex and mannosylated bovine serum albumin for binding to the Mannose receptor of macrophages. Primary culture of peritoneal macrophages were transfected with mannosylated poly-L-lysine conjugated to SV40/luciferase DNA (T). Prior to the addition of the DNA complex a 100-fold excess mannosylated bovine serum albumin was added to one set of plates (Tc). Non-transfected controls (NT) were also assayed for luciferase activity 24 hours after transfection. The luciferase activity is plotted as Relative Luciferase Activity after being standardized relative to the activity found in untransfected controls. Data are expressed